EFFICACY REVIEW

PRODUCT:	Premise 75 Insecticide; Premise 2 Insecticide, Premise 0.5 SC, Premise Pro Insecticide
REG. NUMBER:	432-1332, 432-1331, 432-1362, 432-1449
DATE:	July 19, 2007
DP BARCODE:	D340051, D341481, D341482, D341483
DECISION NUMBER:	379229
GLP:	No
CHEMICAL:	Imidacloprid (75%)
CHEMICAL NUMBER:	129099
PURPOSE:	Provide efficacy data to support the addition of label claims.
MRID:	47130201. Brill, J. (2007) Claim Substantiation Report/ Summery of Product Performance Data to Support Marketing Claims on Premise Termiticide Product: Premise 75 Insecticide, Premise 2 Insecticide, Premise 0.5 SC, and Premise Pro Insecticide. Project Number: JFB051107. Unpublished study prepared by Bayer Crop Science LP. 132 p. 47130202. Sabbagh, G.; Lenz, M.; Fisher, J.; et. al., (2002) Significance of Binding on Imidacloprid Degradation in Soils, and Effects of Soil Characteristics on Imidacloprid Adsorption Capacity. Project Number: 200327. Unpublished study prepared by Bayer Corp., 37 p.
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7-19-07

BACKGROUND:

To support the addition of a long list of claims, divided into categories functional claims, non-repellency claims, insecticidal claims and transfer (domino effect) claims, the registrant has submitted the two MRID's referenced above.

DATA REVIEW:

The following data review is comprised of explanations of materials and methods, and a summation of experimental results containing tables with reformatted data.

47130201. Brill, J. (2007) Claim Substantiation Report/ Summery of Product Performance Data to Support Marketing Claims on Premise Termiticide Product: Premise 75 Insecticide, Premise 2 Insecticide, Premise 0.5 SC, and Premise Pro Insecticide. Project Number: JFB051107. Unpublished study prepared by Bayer Crop Science LP. 132 p.

Appendix 1

Florida (laboratory trials):

The experimental design consisted of exposing dyed termite workers [donors] (*Reticulitermes flavipes*) to soils containing 1000, 100, 10, 1, 0.1, and 0 ppm of imidacloprid for one hour and then placing them into Petri dishes containing untreated soil and 100 unexposed termites [recipients]. A moist piece of filter paper was placed over the soil to act as a food source. Observations on mortality were recorded at 1, 2, 4 and 7 days. Each rate of imidacloprid was replicated 3 times.

Results:

Table 1. Percent Mortality of 100 Recipient Termites After Being Cohabitating with 5 Donor Termites (Florida)

Concentration	1 Day	2 Days	4 Days	7 Days
1000 ppm	12.7	42.7	100	100
100 ppm	1.7	3.3	73.3	95
10 ppm	0	0	7	53.3
1 ppm	1	0.7	4	90
0.1 ppm	0	4	21.7	54.3
Control	0	0	1.3	2

After seven days of cohabitating with 5 donor termites, the percent mortality of the recipient termites ranged from 100 (1000 ppm) to 53.3 (10 ppm).

North Carolina (laboratory trials):

The experimental design consisted of exposing termite workers (donors) to soils containing either imidacloprid at 50 ppm, fipronil at 60 ppm, chlorfenapyr at 125 ppm, and thiamethoxam at 60 ppm for two hours and then placing five termites into Petri

dishes with 25 unexposed recipient termites. A moist piece of filter paper was placed over the soil to act as a food source. Observations on mortality were recorded daily for 7 days.

Results:

Table 2. Percent Mortality of Recipient Termites After Being Exposed to Donor Termites (North Carolina)

Concentration	1 Day	2 Day	3 Day	4 Day	5 Day	6 Day	7 Day
Imidacloprid- 50 ppm	0.5	1.0	35.5	75.0	92.5	93.5	94.5
Fipronil- 60 ppm	0	7.5	93.5	99.9	100	100	100
Thiamethoxam-60 ppm	1.5	2.5	4.0	8.5	27.0	31.0	42.0
Chlorfenapyr-125 ppm	0	2.5	2.5	10.0	23.0	24.5	39.8
Untreated	1.0	1.0	1.0	1.0	5.5	6.5	17.5

The percent morality of recipient termites cohabitating with donor termites exposed to soil treated with imidacloprid ranged from 0.5 (1 day) to 94.5 (7 day).

Appendix 2

Primary Exposure-

The experimental design consisted of exposing termite workers (donors) to soils containing either Premise at 50 ppm, Termidor at 60 ppm, Phantom at 125 ppm, and thiamethoxam at 60 ppm for two hours. Moist filter paper was added to half of the arenas to promote feeding, resulting in primarily dermal acquisition of the termiticides (replicated 5 times). Filter paper was not added to the other arenas to encourage a dermal and oral dose of the termiticides (replicated 10 times). Following the 2 hours of exposure, donor termites were removed and placed into arenas containing moist filter paper and 25 unexposed (recipient) termites. Observations on mortality of the donor termites were recorded daily for 7 days.

Results:

Table 3. Percent Donor Termite Mortality; Dermal Primary Exposure

	1 DAT	2 DAT	3 DAT	4 DAT	5 DAT	6 DAT	7 DAT
Premise	0	0	8	12	12	12	16
Phantom	4	4	4	4	4	4	8
Termidor	0	24	72	80	80	96	100
Thiamethoxam	0	8	24	36	44	52	60
Control	0	4	4	8	8	12	12

The percent mortality of donor termites exposed to Premise (via dermal exposure) ranged from 0% (1 and 2 DAT) to 16% (7 DAT).

Table 4. Percent Donor Termite Mortality; Oral/Dermal Primary Exposure

	1 DAT	2 DAT	3 DAT	4 DAT	5 DAT	6 DAT	7 DAT
Premise	4	94	96	96	96	96	96
Phantom	0	4	4	10	20	24	44
Termidor	8	96	100	100	100	100	100
Thiamethoxam	0	10	12	22	38	40	46
Control	0	2	2	2	12	14	20

The percent mortality of donor termites exposed to Premise (via oral/dermal exposure) ranged from 4% (1 DAT) to 96% (4 – 7 DAT).

Secondary & Tertiary Exposure-

The experimental design consisted of introducing 5 primarily exposed donor termites to Petri dishes containing 25 unexposed termites (secondarily exposed). After 24 hours 5 secondarily exposed termites were removed and placed into Petri dishes containing 20 unexposed termites (tertiary exposure). Observations on mortality were recorded for both secondarily and tertiary exposed termites.

Results:

Table 5. Percent Mortality; Secondary Exposure[1]

	1 DAT	2 DAT	3 DAT	4 DAT	5 DAT	6 DAT	7 DAT
Premise	.5	1	35.5	75	92.5	93.5	94.5
Phantom	0	2.5	2.5	10	23	24.5	39.5
Termidor	0	7.5	93.5	100	100	100	100
Thiamethoxam	1.5	2.5	4	8.5	27	31	42
Control	1	1	1	1	5.5	6.5	17.5

[1] original donor termites exposed via oral/dermal exposure

The percent mortality of termites secondarily exposed to Premise ranged from .5% (1 DAT) to 94.5% (7 DAT). It should be noted that an unacceptable level of control mortality (17.5%) was observed after 7 days.

Table 6. Percent Mortality; Tertiary Exposure[1]

	1 DAT	2 DAT	3 DAT	4 DAT	5 DAT	6 DAT	7 DAT
Premise	0	0	0	0	0	6	14.5
Phantom	0	0	0	9	12	22.5	40
Termidor	0	0	0	18.5	25.5	40	57.5
Thiamethoxam	0	0	0	0	0	2	4.5
Control	.5	.5	.5	.5	.5	.5	19

[1] original donor termites exposed via oral/dermal exposure

The percent mortality of termites exposed (tertiary exposure) to Premise ranged from 0% (1 – 5 DAT) to 14.5% (7 DAT). It should be noted that an unacceptable level of

control mortality (19%) was observed after 7 days.

Appendix 3

This appendix contained favorable quotes concerning the transfer of imidacloprid through termites from publications completed by Drs. Barbara Thorne and Nancy Briesch, Guy Shelton and Ken Grace, and Weste Osbrink and Alan Lax.

Appendix 4

This appendix was comprised of a publication completed by Mike Tomalski and Edward Vargo from North Carolina State University. Experiments were conducted to determine how much imidacloprid is transferred from contaminated to uncontaminated individuals. The experimental design consisted of exposing donor termites to 50 ppm imidacloprid sand for 48 hours and then placing them into arenas containing recipient termites (2:1, 4:1, and 8:1 donor to recipient ratios). Eight recipients were used per ratio. After 24 hours, all termites were individually crushed to determine the amount of imidacloprid they contained. Observations on behavior were also recorded.

Results:

The untreated workers were observed grooming the treated workers. The amount of imidacloprid within the recipients increased with increasing ratio.

Appendix 5

This appendix was comprised of a publication completed by Thomas Shelton and J. Kenneth Grace from the University of Hawaii. Experiments were conducted to determine the potential of nonrepellent termiticide toxicants between Formosan termite (*Coptotermes formosanus*) workers. The experimental design consisted of introducing groups of 30 worker termites to sand containing 0, 1, 10, or 100 ppm imidacloprid or fipronil for 1 hour. Later five contaminated donor termites were introduced to arenas containing recipient termites. Observations on mortality were recorded. There were 3 replicates per treatment.

Results:

Table 7. Percent Mortality of Donor & Recipient Termites Exposed to Termiticide

	Recipient 1 ppm	**Donor 1 ppm**	**Recipient 10 ppm**	**Donor 10 ppm**	**Recipient 100 ppm**	**Donor 100 ppm**
Premise	6.9	37.8	8.7	84.4	61.5	100
Termidor	7.7	35.6	6.4	35.5	38.6	97.8

The percent mortality of recipient termites cohabitating with donor termites exposed to Premise ranged from 6.9% (1 ppm) to 61.5% (100 ppm).

Appendix 6

This appendix was comprised of a publication by Barbara Thorne and Nancy Breisch from the University of Maryland. "Experiments were conducted to determine whether subterranean termites, *Reticulitermes virginicus* (Banks), previously exposed to sublethal doses of imidacloprid (Premise), and allowed to recover for 1 wk, demonstrated behavioral aversion to a subsequent exposure." Observations on termite behavior were also taken.

Results:

Review of the data indicated that surviving worker Formosan termites exposed to Premise tunneled significantly less than their non-exposed counterparts, however showed no apparent aversion to a second encounter with imidacloprid.

It should also be noted that more than 40% of the unexposed termites showed signs of impairment (slow, staggering). The author suggested these symptoms were due to transfer of imidacloprid from exposed termites to unexposed termites.

Appendix 7

This appendix was comprised of a publication by Weste Obsbrink and Alan Lax. The experimental design consisted of periodic sampling of 87 monitors (divided into 8 sectors), initially active with Formosan termites. The monitors were located at varying distances, ranging from 1 to 46 meters, from trees treated with 0.1% Premise foam.

Results:

Although Premise tree treatments did not control Formosan populations (6 sectors recovered after 6 months, while another recovered after 15), imidacloprid-intoxicated termites were observed in monitors 46 meters from the treatment site.

Appendix 8

This appendix was comprised of a publication by Vince Parman and Edward Vargo from North Carolina State University. The experimental design of this ongoing study consisted of genetically identifying the different colonies of termite surrounding 12 termite infested houses. Prior to treatment, each site was heavily monitored to develop maps showing termite location and activity across the property. Each structure was treated with Premise 75 WSP at 0.05%.

Results (initial four homes only):

Table 8. Activity of Subterranean Termite Colonies In & Around Structures

	# Soil Monitors	# Colonies in Monitors	# Colonies In Structure	# Days for Interior Activity to Cease
House 1	77	5	1	21
House 2	89	4	1	7
House 3	54	2	2	45
House 4	60	8	2	85

Review of the data indicates that multiple termite colonies can be surrounding/attacking the same structure. The number of days for interior activity to cease ranged from 7 (house 2) to 85 (house 4).

Appendix 9

This appendix was comprised of a published article (Pest Control; February 2004) concerning the use of genetic markers as tools to study termite biology and assess colony-level effects of termiticides. The article cited the publication referenced in appendix 8.

Appendix 10

This appendix was comprised of a published article (Pest Control; May 2004) concerning the transfer (chain reaction) of termiticides between termites. The article cited the publications referenced in appendices 5, 6, 7 and 8.

47130202. Sabbagh, G.; Lenz, M.; Fisher, J.; et. al., (2002) Significance of Binding on Imidacloprid Degradation in Soils, and Effects of Soil Characteristics on Imidacloprid Adsorption Capacity. Project Number: 200327. Unpublished study prepared by Bayer Corp., 37 p.

The objective of this submission was to demonstrate the behavior of imidacloprid in the soil and to identify the parameters affecting degradation and adsorption characteristics of the compound.

RECOMMENDATIONS:

Functional Claims:

1. Premise can be applied using many different formulations and application methods, making it the most versatile product available for termite control.

- This claim is unacceptable and must be deleted from the label or revised to read "*Premise can be applied using many different formulations and application methods.*"

2. The active ingredient in Premise (imidacloprid) is the most widely used insecticide in the world.
   - This claim is unacceptable and must be deleted from the label.

3. You can trust Premise to protect your home. Over ten years of use, in the US, has proven that Premise can offer unsurpassed protection.
   - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

4. Your pest management professional trusts Premise to protect your home and you can too.
   - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

5. Premise has been used to protect millions of homes from termite attack.
   - This claim is unacceptable and must be deleted from the label.

6. Premise has been widely used, in the US, for over 10 years now with a proven track record for protecting structures from termite attack.
   - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

Claims of non-repellency:

1. Premise is a non-repellent insecticide.
   - acceptable

2. Premise was the first non-repellent insecticide offered for termite control.
   - This claim is unacceptable and must be deleted from the label.

3. Insect can not detect the presence of Premise.
   - This claim is unacceptable and must be deleted from the label or revised to read "*Listed insects can not detect the presence of Premise.*" or "*Termites and ants can not detect the presence of Premise.*"

4. The active ingredient in Premise (imidacloprid) is non-repellent meaning that insects can not detect where the active is applied.
   - This claim is unacceptable and must be deleted from the label or revised to read "*The active ingredient in Premise (imidacloprid) is non-repellent meaning that listed insects can not detect where the active is applied.*" or "*The active ingredient in Premise (imidacloprid) is non-repellent meaning that termites and ants can not detect where the active is applied.*"

5. As a non-repellent, termites can not detect the presence of imidacloprid, at the upper or lower range of parts per million in the soil.
    - This claim is not acceptable and must be deleted from the label.

6. Premise is a non-repellent insecticide – *insects* don't know it is there, so they readily enter treated areas and become exposed.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

7. Research has demonstrated that many insects can not detect the presence of Premise in soil or on surfaces. This is important in that insects do not avoid treated areas – become exposed and are controlled.
    - This claim is unacceptable and must be deleted from the label or revised to read "*Listed insects can not detect the presence of Premise in soil or on surfaces. This is important in that listed insects do not avoid treated areas – become exposed and are controlled.*" or "*Termites and ants can not detect the presence of Premise in soil or on surfaces. This is important in that termites and ants do not avoid treated areas – become exposed and are controlled.*"

8. Premise is non-repellent to insects, which means that insects can not detect and avoid those areas where applied. Non-repellent products offer many advantages over repellent where insects detect the toxicant and avoid the areas.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

9. Termites can not detect the presence of Premise (Imidacloprid) in the soil; therefore they readily enter treated areas and become exposed.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

10. Non-repellent insecticides, like Premise, offer benefit, over repellent products, because insects do not avoid treated areas – become exposed and are controlled.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

11. Many insects have the ability to detect pesticides that are introduced into their environment. The active ingredient in Premise (Imidacloprid) is not detected by insects, meaning that insects readily enter into treated areas and become exposed.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

12. The biggest challenge with protecting structures, from termite attack, is to stop the millions of termites that could be foraging around the structure. Repellent termiticides rely on a perfect barrier to keep termites away, which is very hard to

accomplish. Protection with Premise doesn't rely on a perfect barrier as termites are killed rather than repelled.

- This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

Insecticidal Claims:

1. For prevention or control of subterranean termites, drywood termites, dampwood termites, carpenter ants, and other wood-infesting insects.
   - acceptable

2. Premise controls all native and imported subterranean termite species.
   - acceptable

3. Premise is effective against subterranean termites in the genera Reticulitermes, Coptotermes, Heterotermes and Zootermopsis.
   - acceptable

4. Premise controls drywood termites.
   - acceptable

5. Premise controls wood-destroying beetles.
   - acceptable

6. The long-lasting residual delivers effective termite and ant control.
   - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

7. Premise delivers a dramatically lower retreat rate than pyrethroids.
   - This claim is unacceptable and must be deleted from the label.

8. You can expect to retreat less than 1% of treated homes within the five years after treatment.
   - This claim is unacceptable and must be deleted from the label.

9. The active ingredient in Premise (imidacloprid) has been proven to provide effective control on a broad range of pests, including termites and ants.
   - This claim is unacceptable and must be deleted from the label or revised to read "*The active ingredient in Premise (imidacloprid) has been proven to provide effective control of termites and ants.*"

10. Premise will provide years of protection from termite attack.
    - This is considered a heightened efficacy claim and must be deleted from the label.

11. The active ingredient in Premise (imidacloprid) has been proven to affect termites at extremely low levels in the soil.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

12. Research has shown that Premise affects termites, at very low levels of concentration in the soil. High concentrations of Premise will kill termites quickly, while lower concentrations also kill, but more slowly. This is an important attribute of Premise in that termites, exposed to these lower concentrations will die more slowly allowing time for them to return to the colony and pass the toxicant on to other termites.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

13. The active ingredient in Premise (Imidacloprid) is unique in that when applied to the soil it moves with the water and then binds to the soil, so it won't wash away. This is ideal, with a termiticide, in that the product initially moves, to fill in gaps, but then lock into place to provide the long-term protection that is needed.
    - This claim is unacceptable and must be deleted from the label. The problematic portions have been underlined.

Transfer or "Domino Effect" Claims:

The submitted data do not support transfer or "domino effect" claims. Although some degree of transfer was recorded (between original donor termite and recipient termite) the overall impact/importance is questionable (the percent mortality via tertiary exposure was very low). To have these claims added back on in the future, additional data showing adequate percent mortality via tertiary exposure (or greater) must be submitted in addition to data illustrating the overall impact to the colony over time.

Additionally, efficacy data must be submitted or cited to support any transfer claims for ants.

The following claims must be deleted from the label:

1. Premise controls termites in three ways:
    - Termites tunnel through treated soil – ingest the toxicant and are killed.
    - Termites directly contact the toxicant, while foraging, and are controlled from exposure to their bodies.
    - Termites are social insects in that they care for one another through grooming, nursing and the passing of food. Termites transfer the toxicant from insect to insect becoming exposed. In this way, one exposed termite can expose others to the toxicant. With Premise we refer this as the Domino Effect.

2. Premise transfers throughout the colony by ingestion and contact so effectively that it eliminates entire termite populations in as few as seven days. It's this Domino Effect of Premise that turns termites into killing machines.

3. Domino Effect transfers Premise to untreated areas and maximizes control of all ant and termites species.

4. Termites walk or tunnel through treated areas, then carry Premise back to their nest mates. This way, one termite can help kill hundreds of others. That's the power of the Domino Effect.

5. Premise is carried back to the colony by termites that have entered the Treated Zone.

6. Because termites constantly interact, a lethal dose is transferred to other termites through social interaction and cannibalism.

7. As with termites, the Domino Effect turns foraging worker ants into lethal carriers as they unknowingly take Premise back to their colonies.

8. Research has shown that the active ingredient in Premise (imidacloprid) can be passed from an exposed termite to an unexposed termite through their normal social activities, such as grooming and the passing of food.

9. Premise offers the Domino Effect in that termites that become directly exposed can pass the toxicant on to other termites that have not been directly exposed. This is an important mechanism for controlling termites as many termites never leave the colony. Termites that have foraged into treated areas carry the toxicant back to the colony.